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Case report

Pesticidal suicide: Adult fatal rotenone poisoning

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ABSTRACT

Rotenone is a pesticide and a piscicide derived from the derris root. The mechanism for the cytotoxicity is at mitochondrial level affecting cellular respiration. A suicide by rotenone poisoning in an adult is described. An innovative laboratory methodology was developed for the principal requirement of the Coroner to determine a positive or negative result to assist in the investigation of the death. The ante-mortem concentrations detected were 4.05 ng/ml [0.00405 ppm] in the blood and 0.55 ng/ml [0.00055 ppm] in the serum. Toxicity in human is rare and therefore the interpretation of the toxicology results is complicated by the unavailability of a data bank. The cause of death was attributed to rotenone toxicity based on the circumstantial evidence and expert pathological opinion on a balance of probability acceptable under the Coroners Act 1988 and Coroners Rules 1984 in England and Wales. The forensic clinicopathology of rotenone toxicity is discussed.

1. Introduction

Rotenone is an alkaloid pesticide and piscicide derived from the derris root or stem.[1,2] The pesticide effect of rotenone is relatively non-toxic or moderately toxic to humans.[3] The toxic effect in man was described in a remote tribe who habitually committed suicide by eating derris root.[4] Human fatalities are rare, perhaps because rotenone is available in weak1% to 5% concentration and the dosage is further diluted by the hyperemesis that it induces.[2] Additionally, the rotenone compound is metabolised effectively by the liver.[1] The mechanism of cytotoxicity is the inhibition of mitochondrial cytochrome oxidase and cellular respiration.[5]

The symptoms and signs of rotenone toxicity vary and include nausea, vomiting, incoordination, convulsions, central nervous depression and respiratory distress, bradycardia and arrhythmia.[6] In occupational exposure to derris dust the hazards include conjunctivitis, contact dermatitis and sore throat and the toxicity is potentiated by inhalation of very small dust particles.[2]

This case report of rotenone poisoning involved a human adult. A previous case report of rotenone fatality published almost twenty five years ago involved a child and the manner of death was accidental.[3] A more recently published case of adult fatality after deliberate rotenone ingestion provides a discussion of the critical care therapy and toxicology.[7]

2. Case report

RS was a 47 year old married Indian woman. She had type 2 diabetes mellitus and was on biguanide (metformin 500 mg) treatment. There was no history of depression or suicidal ideation. She was witnessed after a domestic argument to be coughing and vomiting in the bathroom. She was able to walk to her bedroom afterwards with no untoward signs. She was later found having difficulty breathing, on her bed. It transpired that she had ingested rotenone purchased by her husband for use as insecticide in his vegetable garden. She was taken to hospital by ambulance. She received intensive medical care and survived 72 h without regaining consciousness.

On admission to the hospital she had minimum Glasgow Coma Scale (GCS 3/15), hypotension (BP 104/64 mmHg), acidosis (pH7.09) and respiratory distress. A metformin provoked lactic acidosis was excluded on the basis of blood lactate assay and no prescribing contradictions. Her diabetes was stable enough to discount diabetic ketoacidosis. An intracranial catastrophe was suspected initially.

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		Day 1		Day 2		Day 3		Day 4
		2350	0600	0930	1530<	0600	0900	0600
Na^+	135-145 mmol/L	139	142	135	153	148	144	144
K^+	3.5-4.2 mmol/L	4.9	4.1	4.2	4.0	5.0	3.8	3.8
Urea	2.3-6.7mmol/L	2.9	2.7	2.5	1.4	1.3	1.5	1.6
Creatinine	60-125 umol/L	92	67	64	54	59	74	61
Glucose	3.5-8.0 mmol/L	16.8						
Bilirubin (total)	0-20 umol/L	3	3			6		9
Alkaline P	38-109 IU/L	63	51	47		52		57
Alanine A	0-40 IU/L	233	183			122		79
Albumin	35-50 g/L	29	23	26		25		21
Calcium (total)	2.12-2.62 mmol/L	1.91	1.71	1.71		2.2		1.97
Ca^{++}	2.12-2.62 mmol/L	2.1	2.0	1.04		2.45		2.29
Phosphate	0.8-1.5 mmol/L	2.2	0.8	0.4		0.4		1.6
Magnesium	0.7-1.0 mmol/L	0.7	0.57	1.14		0.91		0.66
CRP	0-10 mg/L	4	4			190		193

Fig. 1. Biochemical profile in rotenone Poisoning.

She made some clinical recovery after haemodialysis and correction of the metabolic acidosis. She did not respond to empirical N-acetylcysteine and antioxidant therapy. She was treated with high dose noradrenaline and inotropic sympathomimetics (dobutamine infusion) for the deteriorating multiorgan dysfunction.

The biochemistry and haematology profiles are shown in Figs. 1 and 2. The markedly elevated alanine aminotransferase was consistent with hepatic necrosis and the liver damage was improving with treatment. The results of blood gas analysis could not be retrieved.

3. Postmortem examination

A thanatopsy was conducted some three and a half days after death. The body was that of a well nourished woman, 1.59 m in height and weighed 73 kg (BMI 28). There were various marks of therapeutic intervention. There were no significant marks of violence. The organs showed non-specific general congestion. The relevant observations were mild basal broncho-pneumonia and pulmonary oedema, charcoal gastric content and icteric disintegrating liver with centrilobular hepatic necrosis.

A postmortem toxicology was unsuitable due to the prolonged therapeutic intervention. There were no organs or tissues retained for ancillary tests.

4. Toxicology

The toxicology on antemortem samples obtained during the hospital admission detected rotenone 4.05 ng/ml in the blood and 0.55 ng/ml in the serum and no other drugs including paracetamol. The analysis was basically to determine a positive or negative sample.

The analytic method employed high pressure liquid chromatography (HPLC) with tandem mass spectrometry (MS). A linear curve fit through zero fit was applied with a $1/x^2$ weighting ($r = 0.9963$). The concentrations results were the mean of duplicated determination shown in Fig. 3. The reference standard Rotenone (Pestanal) assumed to be 100% was used for the quantification.

5. Discussion

A quantification of very low concentration of rotenone can be problematic and in the present case an extremely specific and sensitive HPLC with tandem MS technique was employed. The analysis was developed for the principal requirement to determine a positive or negative result for the investigations by the Coroner. The assay was not validated as the analytes were unlikely to be needed for reanalysis. Thus, no information normally generated as part of the validation process is available.

The blood rotenone concentration of 4.05 ng/ml [0.00405 ppm] is far below the single reported result of 2.4 ppm [2400 ng/ml] in a 3½ year old girl who survived for about 8 h.[3] The rotenone in that case was detected by HPLC with variable wavelength and ultraviolet detector in other biological tissue which showed variable distribution in the low range 2–4 ppm in the blood, liver and kidney and none in the brain, muscle and thymus.[3] The lethal dose extrapolated from animal studies is about 0.3–0.5 g/kg in man.[8]

A comparatively low antemortem concentration of rotenone in the present case may be explained by presumptive toxic effect aggravated by preexisting impaired hepatic metabolic pathway in diabetics, unsubstantiated factors such as idiosyncratic reaction, degree of acquired tolerance, larger volume of distribution in an adult and variance in sample collection times and anatomical sites apart from and lack of postmortem drug diffusion or release from a depot into body fluids and redistribution in the tissue. The remarkable difference between the rotenone concentrations in the blood and serum could be the result of unsynchronised collection times of the samples in the hospital and the phenomenon of

		Day 1		Day 2		Day 3		Day 4
		2350	0600	0930	1530<	0600	0900	0600
Hb	11.5-17.5 g/dL	10.9	11.6			10.3		9.0
WBC	4-11x10^9/L	24.2	23.6			12.6		10.9
Platelets	150-400x10^9/L	237	299			171		134
INR	0.8-1.3	1.0	1.2		1.1	1.0	1.1	1.0
APTR	0.8-1.2	0.8	4.0	2.2	1.2	2.9	1.3	1.5
Fibrinogen (derived)	1.9-5.3 g/L	1.5	1.6		3.2	4.3	4.3	4.6

Fig. 2. Haematological profile in rotenone Poisoning.

Sample number	Sample name	Analyte concentration	Calibrated concentration	Accuracy
1	Cal 1 blood	10.0 ng/ml	11.2 ng/ml	112.2 %
2	Cal 2 blood	5.0 ng/ml	4.7 ng/ml	93.1 %
3	Cal 3 blood	2.5 ng/ml	2.4 ng/ml	94.7%
4	Cal 4 blood	0 ng/ml	0 ng/ml	
5	Patient blood		3.9 ng/ml	
6	Patient blood		4.2 ng/ml	
7	Patient serum		0.5 ng/ml	
8	Patient serum		0.6 ng/ml	

Fig. 3. Toxicological profile in rotenone Poisoning.

uneven distribution in the whole blood or red blood cells and serum or plasma since rotenone is known to be very lipophilic and insoluble in water, although there is scant information about the distribution of rotenone.

The interpretation of the toxicology results was complicated by non-availability of data on rotenone toxicity in human, akin to other rare chemical deaths where the tabulated reference range is not well established. The author has previously reported cases illustrating another difficulty in that the statistically compiled lethal range of a compound, based out of necessity on reported fatal cases, serves merely as guidance and this is evident in regular drug overdose cases where victims may survive a death-defying concentration or succumb to a subtherapeutic dose as a result of confounding factors. For practical purpose, the mutual antagonism of these presumed factors should theoretically even out the toxicological artefact but it is emphasised that a proper interpretation of the toxic analytical results should require proper consideration of the circumstances surrounding the death in every case.

In the previous case of the young girl, she had swallowed a mouthful of insecticide containing 6.1 g of rotenone estimated to be equivalent to a lethal dose of 40 mg/kg and the symptoms were emesis, drowsiness, irregular and slowed respiration with progression to deep coma, anuria and acidosis (pH6.76).[3] In the present case, the symptoms were non-specific and generic to a variety of poisoning and the actual volume of insecticide ingested could not be evaluated because of a loss through vomiting and the rotenone container accompanying the patient was disposed by the hospital prior to analysing the volume, purity and strength of the solution.

The mode of death reported in the young girl was cardiopulmonary failure and the necropsy had shown haemorrhages in the gastric submucosa, lungs, heart and thymus, serohaemorrhagic pleural effusion and ascites, juxtamedullary renal congestion and hypoxic brain damage.[3] In the present case, the significant necropsy feature was severe hepatotoxicity without the haemorrhagic component. In the suicide cases of the tribesmen who ate the derris root the stomach was empty of the chewed root expelled by the vomiting and the only change at necropsy was acute congestive cardiac failure.[4]

Tissue samples for histopathology were not obtained because of the constraints under the Coroners Act 1988, Coroners (Amendment) Rules 2005, Coroners Rules 1984 and the Human Tissue Act 2004 in England and Wales that restricts ancillary tests.[9] In any event, the hepatic pathology was visible and microscopy to elucidate acute renal tubular necrosis or cerebral hypoxia which could be a feature of prolonged hypotensive episode would not be diagnostic of rotenone toxicity. In a similar way, the lactic acidosis in rotenone toxicity could be a by product of the cytotoxic anoxia instead of a complication of biguanide therapy that is often associated with renal impairment.

A fact that the deceased in the case presented had ingested a quantity of rotenone is certain and confirmed by the detection in the hospital samples of blood and serum available for toxicological analysis. The cause of death was attributed to rotenone toxicity on 51% balance of probability admissible in the coroner's court. Since a cause of death is an expert pathological opinion and not a matter of fact, the coroner may modify the cause of death after careful consideration of other evidence submitted at the inquest and thereafter reach an appropriate verdict accordingly.[10] The coroner recorded a verdict to a standard of proof beyond reasonable doubt that she took her own life (suicide).

It is understood that among the women folk in the Indian subcontinent there is a cultural belief that recovery after self-poisoning from readily available pesticides will solve domestic strife and the family will live happily ever after.

Conflict of interest
None declared.

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Ethical approval
None.

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Statutes

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